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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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In re application of: Affymetrix, Inc. (William A. Lyon, et al.) )  
Application No.: 09/687,932 )  
Filed: October 13, 2000 )  
For: METHODS AND COMPOSITIONS FOR )  
DETECTING SIGNALS IN BINDING ASSAYS )  
Examiner: B. L. Sisson )  
Attorney Docket: 04537.017 / 3354 )

Art Unit: 1655

#10  
Hedley  
11/30/01

RESPONSE TO OFFICE ACTION

Assistant Commissioner for Patents  
Box OFFICE ACTION RESPONSE  
Washington, D.C. 20231

Mr. Sisson:

Applicant has received an Office action with a mailing date of June 06, 2001 (Paper no. 7).  
This Office action response is intended to be fully responsive to each of the points made by the  
Examiner in the Office action.

**Remarks**

The numbered paragraphs of the Office action are responded to through the corresponding  
numbered paragraphs below. The applicant has addressed each issue in turn and, for clarity, has  
provided a heading for each issue.

Election/Restrictions

- Applicants appreciate Examiner's acknowledgement of Applicants election of Group I,  
claims 1-14 and 19-22. Applicant believes no further response is necessary.

*Claim Rejections – 35 USC §112*

2. The Examiner provided the citation to 35 U.S.C. §112, 1<sup>st</sup> paragraph, that forms the basis for the lack of enablement rejection as set forth in this Office action. Paper no. 7, p. 2.

Applicants respectfully traverse the rejection of claims 1-14 and 19-22 under 35 U.S.C. §112, 1<sup>st</sup> paragraph. Applicants respectfully disagree with Examiner's finding of lack of enablement based upon a need for undue experimentation. Applicants respectfully assert there is no need for undue experimentation to enable the invention. To the contrary, the application enables a person of skill in the art to make and use the invention without undue experimentation. MPEP 2164.01.

Applicants appreciate Examiner's recitation of the elements considered in determining the need for undue experimentation. Applicants restate these for ease in reading Applicants' response. The elements of undue experimentation are: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance provided; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; and (g) the breadth and scope of the claims. Paper no. 7, p. 2; *see also, In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988); *see also*, MPEP 2164.01(a). In analyzing each of these elements, it is necessary to consider all of the evidence related to each of the factors. MPEP 2164.01(a).

*The Quantity of Experimentation Necessary*

The Examiner asserts the quantity of experimentation is great. Paper no. 7, p. 3. Applicants respectfully disagree. Experimentation may be complex if the art typically engages in such experimentation, as long as it is not undue. MPEP 2164.01. Examiner notes that the applicable

person of ordinary skill in the art is one holding a Ph.D. in biochemistry. Paper no. 7, p. 6. Applicants respectfully assert that some experimentation may be required by such a person, however not an inordinate (or undue) amount, and definitely not on the order of several man-years. In addition, one skilled in the art is likely to expect some experimentation. The use of a nucleic acid array is well characterized and has been for some years. Evidence for this fact is shown in the references that are incorporated in the specification and by virtue of the fact that nucleic acid arrays have been commercially available since the mid 1990's.

*The Amount of Direction or Guidance Provided*

Examiner states that the specification is of very limited guidance. Paper no. 7, p. 3. The Examiner also notes a variety of publications are incorporated by reference. Paper no. 7, p. 3. The subject matter required to enable an invention (and therefore, provide guidance) can be found in the application itself and/or the cited prior art. Nucleic acid hybridizations are commonly used in biochemical research and diagnostic assays. The basic foundational elements for enabling hybridizations can be found in the references cited on pp. 7 and 14 of the application. A patent need not teach, and preferably omits, what is well known in the art. MPEP 2164.01. Therefore, the specification need not disclose how these prior art methods are to be adapted so to result in a reproducibly functioning method where a target nucleic acid can be detected using an array of probes with nucleotide sequences of varying length and density, as this is known in the art. Again, the specification details many sources for common techniques in this area (as shown below). *See*, for example, Application, pp. 7, 14, 16-21. Also, nucleic acid arrays have been commercially available through various sources, such as Affymetrix since the mid 1990's.

One skilled in the art would be enabled to practice the invention upon referring to the prior art, in light of the specification.

The Presence of Absence of Working Examples

The Examiner states that only one example is provided and it is entirely prophetic. Paper no. 7, p. 3. Applicants respectfully disagree.

The specification need not contain a working example if the invention is otherwise disclosed in such manner that one skilled in the art would be able to practice the invention without undue experimentation. However, Applicants respectfully assert that a working example is present because reaction conditions and starting materials for multiple embodiments are listed throughout the specification. For example, on p. 3, 2<sup>nd</sup> paragraph, lines 14-17, of the application, the probe is immobilized on a surface, for example the surface being: "Langmuir Blodgett film, glass, germanium, silicon, (poly)tetrafluorethylene, polystyrene, gallium arsenide, gallium phosphide, silicon oxide, silicon nitride, and combinations thereof." In addition, the starting materials and other terms are defined in depth on p. 5 under "Detailed Description of the Preferred Embodiments." Reaction conditions are explained in terms of adjusting the stringency of hybridization, which is known to those of skill in the art. Such factors include, temperature, ionic strength and presence of absence of solvents. Application, p. 7, lines 10-18. These are just a few examples of the starting materials and reaction conditions listed in the specification. Additionally, the many patents and references that are incorporated show many examples of how to run a hybridization reaction.

The Nature of the Invention

The Examiner states the claimed invention requires a heightened level of enablement due to its unpredictable nature. Paper no. 7, p. 4. Applicants recognize physiology and chemistry inventions tend to be less predictable than mechanical inventions and thus require a more detailed specification. However, Applicants respectfully assert that such detail is provided to the extent that one of skill in the art would be enabled to practice the invention without undue experimentation. For example, Applicants have provided information at page 7 of the specification for reference to hybridization reactions, reagents and conditions. There are other references to techniques in the application that show individual technologies of the invention, such as purification, labeling, and ultimate uses of the technology.

The State of the Prior Art

The Examiner asserts that there are a variety of problems cited in the prior art. Paper no. 7, p. 5. It is one of skill in the art that could encounter some problems with hybridization in some circumstances. However, that does not affect the enablement of the presently claimed invention. The specification deals with problems that may be encountered during hybridization by providing both strict and less strict conditions and providing examples of the types of results expected to be achieved from either condition. Application, p. 7, lines 10-18. The application not only recognizes the problems as described in the prior art, it is also drafted to overcome many of these problems. In addition, the application lists multiple embodiments and varying conditions/expectations to address the unpredictability of the physical and chemical arts.

The Relative Skill of Those in the Art

Examiner states the relative skill of those in the art is on par with those that hold a Ph.D. in biochemistry. Paper no. 7, p. 6. Applicants agree that the relative skill of those in the art that is most closely associated with the claimed invention is high. Consequently, the skilled artisan would have available to them the general and specific references that are cited in the application and would know how to perform the recited techniques given the teaching in the specification and the fact that these are techniques that are common in labs.

The Breadth of Scope of the Claims

Examiner states the claims are of sufficient breadth of scope so as to encompass a multitude of problematic conditions recognized in the art. Paper no. 7, p. 6. Applicants respectfully disagree.

For example, Applicants respectfully assert there is no necessity or basis for placing an upper limit on the number of probes or being concerned about the complementarity of probes. Rather, such an upper limit on probes does not affect enablement. *See references*, Application, pp. 19-21. In fact, greater informational content results from a greater number of probes. The arrays shown and described in the specification and references are capable of putting the largest number of probes on an array of any technology available. Consequently, Applicants respectfully assert that this is not a basis for lack of enablement of the presently claimed invention.

The Examiner has discussed crudeness of the sample, probe design, and has made other comments regarding the use of an array. As stated above, one of skill in the art knows how to perform a hybridization reaction with nucleic acids and with nucleic acid arrays. The general techniques have been in practice for several decades and the specific techniques with arrays have been available with commercial products since the mid 1990's. Clearly, these methodologies work.

Consequently, Applicants respectfully assert the specification does indeed speak to how such assays are to be performed by reference to the applicable prior art and statements in the specification. Applicants respectfully assert that the disclosure enables one of skill in the art to make and use the claimed invention without undue experimentation.

***Conclusion***

In view of the foregoing, and in summary, Applicants believe that all issues and points of the Examiner's Office action have been addressed and that claims 1-14 and 19-22 are patentable over the prior art. Reconsideration and allowance of the application is respectfully requested.

Please address all future correspondence related to the above-referenced patent application to:

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Dated this 6<sup>th</sup> day of November 2001.

Respectfully submitted,



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